

The online version of this article has been published under an open access model. Users are entitled to use, reproduce, disseminate, or display the open access version of this article for noncommercial purposes provided that: the original authorship is properly and fully attributed; the Journal and Oxford University Press are attributed as the original place of publication with the correct citation details given; if an article is subsequently reproduced or disseminated not in its entirety but only in part or as a derivative work this must be clearly indicated. For commercial re-use, please contact journals.permissions@oxfordjournals.org
 © The Author 2006; all rights reserved.

International Journal of Epidemiology
 doi:10.1093/ije/dyl214

Letter to the Editor

Genomics, epidemiology, and common complex diseases: let's not throw out the baby with the bathwater!

From MUIN J KHOORY and MARTA GWINN

As public health professionals working to translate advances of genome-based research into population health benefits,^{1,2} we found the article by Buchanan *et al.*³ and associated commentaries^{4–10} fascinating and informative. We too are sceptical of 'genohype' and we are critical of the specious paradigm that leads directly from gene discovery to test development.¹¹ We advocate an evidence-based approach that integrates knowledge from diverse fields—including genetic epidemiology¹²—to assess the clinical utility of genetic information for the benefit of population health.¹³

Therefore, we were astonished and disappointed to encounter Buchanan's summary dismissal of genetic epidemiology as a misguided and hopeless quest for the philosopher's stone. Delivered scarcely 3 years after completion of the Human Genome Project, this judgement is clearly premature. Population-based epidemiological research that makes the most of newly available information and techniques is just beginning. We should expect this research to take time—years, if not decades—to appropriately conduct, analyse, report, and synthesize.

Although we agree that public health programmes should continue to promote a healthy diet, adequate physical activity, and smoking cessation, it makes no sense to assert that 'the preponderance of cases of complex chronic disease are owing to exogenous experience rather than endogenous genetic susceptibility'.¹⁰ Obviously, 'people are not born with complex, late-onset disease'; on the other hand, people who continue to eat too much, spend too much time on the couch and smoke (despite vigorous public health education campaigns) do not always develop heart disease. Clearly, there is much more to learn about gene–environment interactions underlying these diseases and to use this knowledge in intervention efforts.

As we have argued elsewhere,¹⁴ the public health significance of genomic research on common complex diseases with strong environmental determinants lies not in finding new genetic 'causes' of these diseases but in helping us to better recognize and modify interacting environmental risk factors. Each investigation that increases our understanding of gene–environment interaction, etiological heterogeneity, pathogenesis, and natural history of common diseases adds to a knowledge base for estimating risks and guiding

interventions to improve population health. Epidemiology is unique in offering a set of evolving tools and methods that are explicitly designed to observe disease variation in populations and reveal the joint effects of individual biology and behaviour in the context of social and physical environment. In an already complex world, human genetic variation is another dimension that is just now opening for exploration.¹⁵ For epidemiologists to retreat now would be to abandon the field just when they are needed most.

The concerns enumerated by Buchanan *et al.*³—including phenotypic and genotypic heterogeneity, the interplay between individual and ecological variables, the dynamic nature of environmental risk, chance, and bias—are all important and well-recognized challenges in epidemiological research. Nevertheless, we take issue with their assessment that 'the lack of an obvious alternative does not justify continuing to invest in what does not work'. Indeed, there is no obvious alternative to epidemiology for translating genetic information from basic science to population health benefits but the assertion that it has not worked is simply premature. Epidemiology in the genomics era is still a baby. Let's not throw it out with the bathwater.

References

- Gwinn M, Khoury MJ. Genomics and public health in the United States: signposts on the translation highway. *Comm Genet* 2006;**9**:21–26.
- Burke W, Khoury MJ, Stewart A, Zimmern R, The Bellagio working group. The path from genome-based research to population health: development of an international public health genomics network. *Genet Med* 2006;**8**:451–58.
- Buchanan AV, Weiss KM, Fullerton SM. Dissecting complex disease: the quest for the philosopher's stone? *Int J Epidemiol* 2006;**35**:562–71.
- Ioannidis JPA. Commentary: grading the credibility of molecular evidence for complex diseases *Int J Epidemiol* 2006;**35**:572–78.
- Millikan RC. Commentary: The human genome: philosopher's stone or magic wand? *Int J Epidemiol* 2006;**35**:578–81.
- Coggon D. Commentary: Complex disease—responding to the challenge. *Int J Epidemiol* 2006;**35**:581–83.
- Weed DL. Commentary: Rethinking epidemiology. *Int J Epidemiol* 2006;**35**:583–86.
- Schwartz S, Ezra Susser E. Commentary: What can epidemiology accomplish? *Int J Epidemiol* 2006;**35**:587–90.
- Merikangas KR, Low NCP, Hardy J. Commentary: Understanding sources of complexity in chronic diseases—the importance of

National Office of Public Health Genomics, Centers for Disease Control and Prevention, 4770 Buford Highway, Atlanta, GA, USA.

*Corresponding author: E-mail: mkhoury@cdc.gov

- integration of genetics and epidemiology. *Int J Epidemiol* 2006;**35**:590–92.
- ¹⁰ Buchanan AV, Weiss KM, Fullerton SM. Authors' response. On stones, wands, and promises. *Int J Epidemiol* 2006;**35**:593–96.
- ¹¹ Janssens AJW, Gwinn M, Valdez R, Venkat Narayan RM, and Khoury MJ. Predictive genetic testing for type 2 diabetes may raise unrealistic expectations. *BMJ* 2006;**333**:509–10.
- ¹² Centers for Disease Control and Prevention. The Human Genome Epidemiology Network (HuGENet). Available at: <http://www.cdc.gov/genomics/hugenet/default.htm> (Accessed August 15, 2006).
- ¹³ Centers for Disease Control and Prevention. Evaluation of Genomic Applications in Practice and Prevention (EGAPP). Available at: <http://www.cdc.gov/genomics/gtesting/egapp.htm> (Accessed August 15, 2006).
- ¹⁴ Khoury MJ, Davis RL, Gwinn M, Lindegren ML, Yoon PW. Do we need genomic research for the prevention of common diseases with environmental causes? *Am J Epidemiol* 2005;**161**:799–805.
- ¹⁵ Khoury MJ, Millikan R, Little J, Gwinn ML. The emergence of epidemiology in the genomics age. *Int J Epidemiol* 2004;**33**:936–44.